

Heartburn

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Heartburn is the most common symptom of GERD, a chronic and relapsing condition that carries a significant risk of morbidity and the potential for resultant complications. It is defined by symptoms related to mucosal damage produced by abnormal reflux of gastric contents into the esophagus. Population-based studies demonstrate that 40% of U.S. adults experience heartburn monthly, with a 20% age- and sex-adjusted prevalence of weekly symptoms. It is important to also consider emergent causes of heartburn, such as MI in addition to GERD and more chronic conditions.

Most patients with GERD self-treat with OTC medications and do not initially seek medical attention for their symptoms. Health-related quality-of-life surveys reveal that patients with GERD have lower symptomatic assessment scores than patients with CHF, CAD, and diabetes mellitus. GERD is responsible for the highest annual direct costs related to all GI disorders, estimated at more than \$10 billion per year, with the largest component of these costs attributable to antireflux medications, approaching \$6 billion annually.

The vast majority (>90%) of patients with GERD evaluated in primary care practices have nonerosive reflux disease (NERD), whereas a minority will progress to develop erosive esophagitis, and even fewer will develop esophageal strictures, Barrett's esophagus, and adenocarcinoma of the esophagus. Patients with NERD are prone to develop extraesophageal/atypical manifestations (Table 26-1), yet given a small risk of disease progression, they generally do not require long-term surveillance despite persistent reflux symptoms. Symptom relapse rates in patients with NERD are similar to those in patients with erosive esophagitis, and although many patients will require daily pharmacologic treatment to control heartburn, less than 10% will develop erosive esophagitis on upper endoscopy over time.

When a patient exhibits the classic symptoms of heartburn and acid regurgitation, the diagnosis of GERD can be made with high specificity, yet the sensitivity remains low. Evidence for the positive predictive value of heartburn for accurately diagnosing GERD is suboptimal due to the lack of a diagnostic gold standard. Intensity and frequency of reflux symptoms are poor predictors of the presence or severity of reflux esophagitis. The diagnostic workup for determining GERD includes:

Table 26-1. Extraesophageal or Atypical Manifestations of GERD

- Aspiration
- Asthma
- Chronic cough
- Dental enamel loss
- Globus sensation
- Noncardiac chest pain
- Recurrent laryngitis
- Recurrent sore throat
- Subglottic stenosis

Adapted from Heidelbaugh JJ, Nostrant TT: Medical and surgical management of gastroesophageal reflux disease, *Clin Fam Pract* 6:547-568, 2004.

- The Bernstein test—A test infusion into the distal esophagus of either 0.1N HCl or 0.9% NaCl in a single-blinded fashion with an assessment of the patient's response can be used to detect GERD, if a patient's symptoms are directly related to acid reflux (not widely used).
- The 24-hour pH probe—Accepted as the standard for establishing or excluding the presence of GERD, but is often inconvenient to the patient, and lacks the sensitivity and specificity (70% to 96%) required to be a gold standard; more often used in infants and children to accurately diagnose GERD
- Double-contrast barium radiography—Has limited usefulness in making an accurate diagnosis of GERD, but may be useful in defining the presence of anatomic abnormalities, including pyloric stenosis, malrotation, and annular pancreas in the vomiting infant, and hiatal hernia and esophageal strictures in children and adults
- Upper endoscopy or EGD with or without biopsy—The gold standard in assessing esophageal complications of GERD (e.g., erosive esophagitis and Barrett's esophagus), yet lacks an appreciable sensitivity and specificity for identifying pathologic reflux

Symptoms

- Acid regurgitation +++++
- Burning sensation in the throat ++++
- Sour or bitter taste in the mouth (water brash) +++
- Swallowing can be difficult ++
- Belching ++
- Wheezing +

Table 26-2 lists alarm symptoms of GERD that suggest complicated disease and warrant referral to gastroenterology for evaluation.

Signs

- Commonly, none are present in NERD and uncomplicated disease. +++++
- Physical manifestations may include extraesophageal/atypical manifestations (see **Table 26-1**) ++ and alarm symptoms of complicated disease (see **Table 26-2**). +

Table 26-2. Alarm Symptoms of GERD Suggesting Complicated Disease

- Black or bloody stools
- Choking
- Chronic coughing
- Dysphagia
- Early satiety
- Hematemesis
- Hoarseness
- Iron deficiency anemia
- Odynophagia
- Weight loss

Adapted from Heidelbaugh JJ, Nostrant TT: Medical and surgical management of gastroesophageal reflux disease, *Clin Fam Pract* 6:547-568, 2004.

Workup

- If suggested by history and physical examination, CAD should first be ruled out in patients presenting with heartburn.
 - ECG and cardiac enzyme testing initially
 - Stress testing as indicated
- Differential diagnosis
 - CAD—Myocardial infarction and angina pectoris
 - Other acid-related illnesses—Peptic ulcer disease, gastritis, and non-ulcer dyspepsia
 - Esophageal motility disorders—Spasm, achalasia, scleroderma, and radiation injury
 - Infectious esophagitis—*Candida*, herpes, HIV, and cytomegalovirus (CMV)
 - Pill-induced esophagitis—Doxycycline, ascorbic acid, quinidine, potassium chloride, and bisphosphonates
 - Anatomic problems of the esophagus—Strictures, webs, rings, diverticula, atresia, and fistulas
 - Esophageal carcinoma
 - Chemical esophagitis (i.e., lye ingestion)
 - Crohn's disease of the esophagus
 - Biliary tract disease
 - Other esophageal-related problems—Eosinophilic esophagitis, alkaline reflux, Mallory-Weiss syndrome, and Chagas disease
 - Nonesophageal or indirect problems—Myasthenia gravis, pulmonary embolus, muscle strain, asthma, and pregnancy
- History will often reveal causes such as ingestions, medications, or radiation.
- Infectious causes can be suggested by history and physical examination and confirmed by endoscopic visualization and, in some cases serology, or culture.
- Esophageal manometry is useful in confirming motility disorders.
- Abdominal or biliary ultrasonography, double contrast barium swallow, 24-hour esophageal pH monitoring, radionuclide scintigraphy, and EGD complete the diagnostic armamentarium.

Table 26-3. Pharmacologic Therapy for the Treatment of GERD

- Histamine-2 receptor antagonists (H_2 RAs)
 - Cimetidine (Tagamet)
 - Famotidine (Pepcid)
 - Nizatidine (Axid)
 - Ranitidine (Zantac)
 - Proton pump inhibitors (PPIs)
 - Esomeprazole (Nexium)
 - Lansoprazole (Prevacid)
 - Omeprazole (Prilosec)
 - Pantoprazole (Prevacid)
 - Rabeprazole (Aciphex)
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- Diagnostic testing is recommended in patients with GERD who:
 - Have an inadequate response to an empiric trial of antisecretory therapy (e.g., on-demand treatment with PPIs taken 15 to 30 minutes prior to the first meal of the day or histamine-2 receptor antagonists [H_2 RAs] taken daily to twice daily during symptom exacerbations [Table 26-3])
 - Require continuous chronic antisecretory therapy to control frequent GERD symptoms
 - Have chronic reflux symptoms lasting more than 5 years and are thus at an increased risk for esophageal strictures and Barrett's esophagus
 - Have extraesophageal/atypical manifestations suggesting complicated disease (see Table 26-1)
 - Have alarm symptoms suggesting complicated disease or cancer (see Table 26-2)
 - In the absence of alarm signs or symptoms, the diagnosis of GERD can be made with high sensitivity and specificity based on clinical presentation without the need for testing or gastroenterology referral.
 - In the presence of alarm signs or symptoms or extraesophageal/atypical manifestations, upper endoscopy is recommended to rule out complicated or advanced disease.
 - In observational studies, the progression from NERD to severe esophagitis has not occurred in patients with an initial normal endoscopy whose symptoms have remained unchanged during 10-year follow-up, arguing against repeat endoscopy during that time period, in the absence of alarm symptoms.

Comments and Treatment Considerations

Initial empiric pharmacotherapy for treatment of GERD should consist of either a PPI or H_2 RA, and is reasonable without the need for immediate diagnostic testing in the vast majority of cases (Fig. 26-1). In patients who incompletely respond to a trial of either OTC or prescription H_2 RAs, PPIs taken once daily are preferred over continuing H_2 RA therapy due to their greater efficacy and faster symptom control, as well as the limited additional benefit gained from extending

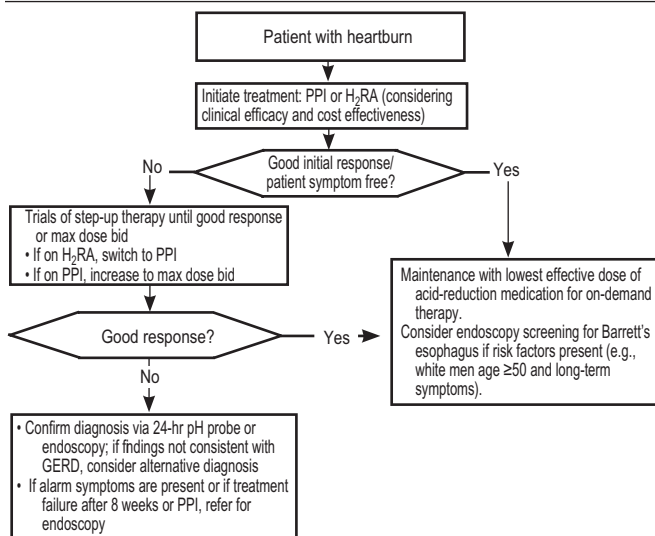


FIGURE 26-1 Algorithm for the diagnosis and treatment of GERD. (Adapted from Heidelbaugh JJ, Gill A, Nostrant TT, Harrison RV: Gastroesophageal reflux disease (GERD), Ann Arbor, MI, 2006, Office of Clinical Affairs, University of Michigan Health System.) H₂RA, Histamine-2 receptor antagonist; PPI, proton pump inhibitor.

therapy with the same or higher-dose H₂RA. Additional benefit may be obtained by extending treatment for another 4 to 8 weeks with either the same or double-dose PPI.

An inadequate response to a 4- or 8-week trial of standard dose PPI may indicate longer treatment is needed, more severe disease, or an incorrect diagnosis. Evidence from RCTs demonstrated improved control of GERD symptoms over a 4- to 8-week period in patients treated with PPIs (83%) compared with those given H₂RAs or placebo (60% and 27%, respectively). A greater percentage of patients treated with PPIs has been found to be in symptomatic remission at 12 months compared with patients who received either H₂RAs or placebo.

In the treatment of erosive esophagitis, faster healing rates have been achieved in patients who received PPI therapy for 4 to 8 weeks (78%) than in patients given H₂RAs or placebo (50% and 24%, respectively) for the same period; at 1 year, patients treated daily with a PPI were significantly less likely to relapse than those who received an H₂RA. Economic analyses of various empiric treatment strategies revealed that an 8-week course of PPIs for initial symptom relief taken on demand is more cost-effective than continuous, step-up/step-down, or intermittent strategies with either H₂RAs or PPIs.

Expert opinion states that lifestyle modifications should be recommended as adjunctive therapy in all patients with GERD (Table 26-4).

Table 26-4. Suggested Lifestyle Modifications for the Treatment of GERD

- Avoid acidic foods (citrus and tomato-based products), alcohol, caffeinated beverages, chocolate, onions, garlic, salt, and peppermint
- Avoid large meals
- Avoid medications that may potentiate GERD symptoms: calcium channel blockers, β -agonists, α -adrenergic agonists, theophylline, nitrates, and sedatives
- Avoid recumbency 3 to 4 hours postprandially
- Avoid tight clothing around the waist
- Decrease dietary fat intake
- Elevate the head of bed 4 to 8 inches
- Lose weight
- Smoking cessation

Summarized from DeVault KR, Castell DO: Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. The practice parameters committee of the American College of Gastroenterology, *Am J Gastroenterol* 94:1434-1442, 1999.

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